RESEARCH ARTICLE

Design and evaluation of the fast dissolving tablet of terbutaline sulfate

Manivannan Rangasamy, Balasubramaniam Ayyasamy, Senthilkumar Raju[1], Sandeep Gummadevelly

Department of Pharmaceutics, J.K.K.M.M.R.F, College of Pharmacy, B. Komarapalayam, Namakkal - 638 183,
[1]Department of Chemistry, Swamy Vivekanandha College of Pharmacy, Elayampalayam, Namakkal, Tamilnadu, India

Asthma is an inflammatory disorder that results in the obstruction of air pathways and causes difficulty in breathing. Oral dosage forms associated with lag time and delayed onset of action are among the available means of treatment. However, aerosols and parenterals have a rapid onset of action but strongly affect the patient compliance. Thus, an attempt was made to improve the onset of action of bronchodilator used commonly in the treatment of asthma. Fast dissolving tablets of terbutaline sulfate were prepared by the direct compression method after incorporating superdisintegrants such as Explotab, Ac-Di-Sol and Polyplasdone XL in different concentrations. The prepared tablets were evaluated for weight variation, thickness, hardness, friability, wetting time, drug content, water absorption ratio, *in vitro* dispersion time, *in vitro* disintegration time and *in vitro* drug release. Among all, the formulation F9 (containing 5% w/w concentration of Polyplasdone XL) was considered to be the best formulation, which releases up to 99.33% of the drug in 10 min.

Key words: *Ac-Di-Sol, direct compression, explotab, polyplasdone XL, terbutaline sulfate*

INTRODUCTION

Over a decade, the demand for the development of fast dissolving tablets has enormously increased as it has a significant impact on patient compliance. Fast dissolving tablets offer an advantage for populations who have difficulty in swallowing. It has been reported that dysphagia[1] is common among all the age groups and more specific with the pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting and motion sickness complications.[2] Fast dissolving tablets with a good taste and flavor increase the acceptability of bitter drugs by various group of the population.

Terbutaline sulfate is a selective β-adrenergic agonist bronchodilator. Chemically, it is (±)-a-[(tert-butylamino) methyl]-3, 5 dihydroxy benzyl alcohol sulfate. It is an effective agent in the treatment of bronchospasm in bronchial asthma and chronic bronchitis.[3] However, the oral bioavailability is poor, with only 14.8% of the dose reaching systemic circulation due to extensive first pass metabolism.

Address for correspondence:
Dr. R. Manivannan, Department of Pharmaceutics, J.K.K.M.M.R.F, College of Pharmacy, Komarapalayam, Pin Code: 638 - 183, Namakkal, Tamilnadu, India.
E-mail: manivannan_biotech@yahoo.co.in

DOI: 10.4103/0973-8398.56300

Hence, an attempt was made for preparation of fast dissolving tablets of model bronchodilator terbutaline sulfate with an aim of reducing the lag time and providing faster onset of action to relieve the acute asthmatic effect immediately.

MATERIALS AND METHODS

Terbutaline sulfate was received as a gift sample from Spic Pharma (Chennai, India). Explotab, Ac-Di-Sol and Polyplasdone XL were obtained from signet chemical corporation, Mumbai, India. Colloidal silicon dioxide and mannitol-D were obtained from Micro Labs, Hosur, India. All other reagents used were of analytical grade.

Preparation of the fast dissolving tablet of terbutaline sulfate

The superdisintegrants (Explotab, Ac-Di-Sol and Polyplasdone XL) in varying concentrations (3-5%) were used to prepare the tablets. All the ingredients [Table 1] were passed through sieve no. 40 and mixed in geometric progression in a dry and clean mortar for 25 min. The mixed blend of excipients was compressed into tablets using 6.93 mm flat beveldeged punches in an 8 station rotary tablet machine[4] (Kambert).

Evaluation of the tablets

The prepared fast dissolving tablets were evaluated for thickness, hardness[5] (Monsanto hardness tester), friability[6] (Roche friabilator), weight variation, drug content,[7,8] wetting time, water-absorption ratio,[9]

in vitro dispersion time and *in vitro* disintegration time. The *in vitro* dissolution studies of fast dissolving tablets were performed using a type-II apparatus as specified in the United State Pharmacopoeia at 50 rpm (Electro Lab, Mumbai, India) and Sorenson's buffer (pH 6.2), 650 ml was used as dissolution medium. Temperature of the dissolution medium was maintained at 37 ± 0.5°C. An aliquot of the dissolution medium was withdrawn at a specific time interval and it was filtered. Absorption of the filtered solution was checked by UV spectroscopy (Shimadzu, Japan) at 276.6 nm and the drug content was determined from the standard calibration curve. Dissolution rate was studied for all designed formulations and the conventional tablet.[10]

RESULTS AND DISCUSSION

The present investigation was undertaken to fabricate and evaluate fast dissolving tablets of terbutaline sulfate by the direct compression method comparing with the conventional tablet. Superdisintegrants at different concentration levels (3, 4 and 5% w/w) were used to assist disintegration.

Bulk densities of various formulations varied between 0.55 and 0.58 g/cm^3. The angle of repose and the compressibility values varied from 21° to 23° and 9.44 to 13.16%, respectively. From these values, it was evident that these blends had excellent flow properties.

Physical parameters conformed to the requirements. Weight variation was found within the specification of the USP limits. Average weight of 20 tablets of all nine formulations was found in the range of 98.9-100.7 mg. Hardness, thickness and friability of all the tablet formulations were observed in the range of 2.14-2.42 kg/cm^2, 2.52-2.55 mm and 0.212-0.276%, respectively. Wetting time and water absorption ratio were found in the range of 9.76-13.48 s and 69.41-81.42%, respectively. Drug content of all the formulations was found in the range of 99.96-100.01%.

The *in vitro* dispersion time of Polyplasdone XL, Explotab and Ac-Di-Sol containing batches were found in the range of 8.79-8.91 s, 11.16-11.27 s and 10.01-10.09 s, respectively. The *in vitro* disintegration time was rapid with Polyplasdone XL containing batches (10.04-10.10 s) and delayed with Explotab containing batches (13.79-13.86 s). The rapid disintegration may be due to the rapid uptake of water from the medium, swelling and burst effect Table 2.

In vitro dissolution studies of various formulations at different time intervals are reported in Table 3. The Polyplasdone XL formulation showed the maximum dissolution rate of 99.33% drug release in 10 min. Ac-Di-Sol containing tablets released more than 97.65% of the drug in 10 min and Explotab formulations released more than 98.12% of the drug in 10 min. This shows that the effectiveness of superdisintegrants was in the order of Polyplasdone XL > Ac-Di-Sol > Explotab.

Table 1: Fof fast dissolving tablet of terbutaline sulfate

Formulation ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Terbutaline sulfate	5	5	5	5	5	5	5	5	5
Explotab	3	4	5	-	-	-	-	-	-
Ac-Di-Sol	-	-	-	3	4	5	-	-	-
Polyoplasdone	-	-	-	-	-	-	3	4	5
Microcrystaline cellulose	30.6	29.6	28.6	30.6	29.6	28.6	30.6	29.6	28.6
Mannitol	54	54	54	54	54	54	54	54	54
Aspartame	5	5	5	5	5	5	5	5	5
Flavor	2	2	2	2	2	2	2	2	2
Aerosil	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Megnesium stearate	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2

Table 2: Evaluation of the fast dissolving tablet of terbutaline sulfate

Formulation parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bulk density (g/cm^3)	0.582	0.583	0.582	0.563	0.561	0.561	0.553	0.554	0.553
Tapped density (g/cm^3)	0.643	0.647	0.646	0.646	0.644	0.646	0.633	0.637	0.631
Hausners ratio	1.104	1.109	1.108	1.148	1.146	1.152	1.145	1.143	1.144
Angle of repose (°)	22.43	22.58	23.52	21.85	21.99	22.32	20.99	21.73	21.70
Compressibility index (%)	9.44	9.89	9.81	12.88	12.90	13.16	12.64	12.52	12.58
Thickness (mm)	2.53	2.52	2.53	2.52	2.51	2.53	2.55	2.53	2.53
Hardness (kg/cm^2)	2.34	2.26	2.16	2.42	2.26	2.14	2.32	2.38	2.22
Friability (%)	0.235	0.226	0.276	0.212	0.251	0.256	0.249	0.234	0.253
Drug content (%)	99.98	99.98	100.01	100.04	100.03	100.01	99.99	99.96	100.01
Wetting time (s)	13.12	13.48	13.39	11.16	11.11	11.16	9.81	9.84	9.76
Water absorption ratio (%)	79.56	79.83	81.42	76.05	75.99	75.52	69.41	70.13	69.56
Dispersion time (s)	11.16	11.27	11.26	10.01	10.06	10.09	8.79	8.90	8.91
Disintegration time (s)	13.83	13.79	13.86	12.08	12.12	12.14	10.10	10.08	10.04

Table 3: *In vitro* dissolution profile of formulations F1-F9 and the conventional tablet

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	Conventional tablet
1	66.45	75.65	77.53	77.67	78.63	79.34	75.97	76.50	82.56	13.26
2	71.38	80.45	83.86	81.56	83.47	84.36	79.32	81.13	86.69	16.26
4	80.79	86.88	88.64	88.64	89.81	88.05	84.15	85.77	91.21	28.47
6	86.19	90.79	93.71	92.13	92.44	94.71	88.47	89.88	95.26	35.23
8	89.56	93.64	96.11	94.36	96.54	97.58	93.26	94.03	97.56	41.63
10	92.74	95.64	97.65	96.73	97.96	98.12	97.19	98.35	99.33	46.12

The comparative reduction in the drug dissolution rate by Explotab was possibly due to the lack of binding force during direct compression. From the overall observations, formulation F9 containing 5% w/w Polyplasdone XL was considered to be the best formulation, which releases up to 99.33% of the drug in 10 min. The *in vitro* drug release profile F9 was compared with conventional tablet. The conventional tablet released only 46.12% of the drug in 10 min whereas the F9 formulation released up to 99.33%.

It can be conclusively inferred that the fast dissolving tablet of terbutaline sulfate with 5% w/w Polyplasdone XL as the superdisintegrant is an alternative to and better than the conventional tablet dosage form used in the management of asthma.

REFERENCES

1. Lindgren S, Janzon L. Dysphagia: Prevalence of swallowing complaints and clinical finding. Med Clin North Am 1993;77:3-5.
2. Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery: A review. Pharm Sci Technol Today 2000;3:138-45.
3. Bradley JU, Lawrence ML. Drugs used in the treatment of asthma. In: Hardman JG, Lee E, editors. Goodman and Gilman's: The Pharmacological basis of therapeutics. 10th ed. New York: The Mc Graw-Hill Companies; 2001. p. 735.
4. Kucherkar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets of salbutamol sulphate: A novel drug delivery system. Indian Drugs 2004;41:592-8.
5. Banker GS, Anderson NR. In: Lachman L, Liberman HA, Kanig JL, editors. The theory and Practice of industrial pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 1987. p. 297.
6. Indian Pharmacopoeia. Vol. 2. Delhi: The Controller of Publications; 1996. p. A-80.
7. Arias MJ, Gines JM, Moyano JR, Perez-Martinez JI, Rabasco AM. Influence of preparation method of solid dispersions on dissolution rate: Study of triammterene-D- mannitol system. Int J Pharm 1995;123:25-31.
8. Yunxia B, Sunada H, Yonezawa Y, Danjo K. Evaluation of rapid disintegrating tablets prepared by direct compression method. Drug Dev Ind Pharm 1999;25:571.
9. Chaudhari PD, Chaudhari SP, Kolhe SR, Dave KV, More DM. Formulation and evaluation of fast dissolving tablet of famotidine. Indian Drugs 2005;42:641-9.
10. Kuchekar BS, Arumugam V. Fast dissolving tablets. Indian J Pharm Edu 2001;35:150.

Source of Support: Nil, **Conflict of Interest:** None declared.